REMARKS

Claims 1-21 are pending in the subject application. Applicant has herein cancelled claims 3, 18 and 21 without prejudice or disclaimer to applicant's right to pursue the subject matter of these claims in the future. In addition, applicants have amended claims 1, 4, 5, 7, 8, 10, 11, 16, 17, 19 and 20. Support for the amendments to claim 1 can be found in the specification as originally filed at, inter alia, page 3, lines 4-21; page 11, lines 1-5; and page 15, lines 3 to 5. Support for the amendments to claim 4 can be found in the specification as originally filed at, inter alia, page 15, lines 16 to 20. Support for the amendments to claim 5 can be found in the specification as originally filed at, inter alia, page 15, lines 28-30. Support for the amendments to claim 7 can be found in the specification as originally filed at, inter alia, page 11, lines 18-22. Claim 8 has been amended merely to correct the term "the" to "an". Claim 9 has been amended merely to correct its dependency. Support for the amendments to claim 10 can be found in the specification as originally filed at, inter alia, page 12, lines 5-24; and at page 15, lines 3-5. Support for the amendments to claim 11 can be found in the specification as originally filed at, inter alia, page 12, lines 25-30. Support for the amendments to claim 16 can be found in the specification as originally filed at, inter alia, page 13, lines 24-29. Support for the amendments to claim 17 can be found in the specification as originally filed at, inter alia, page 14, lines 1-5. Support for the amendments to claim 19 can be found in the specification as originally filed at, inter alia, page 14, lines 10-16. Support for the amendments to claim 20 can be found in the specification as originally filed at, inter alia, page 14, lines 17-21. Applicant maintains that the amendment to

the claims raises no issue of new matter. Accordingly, applicant respectfully requests entry of this Amendment.

Specification

In the June 28, 2006 Office Action the Examiner indicated that sequences are disclosed on page 19 of the specification which are not listed in the Sequence Listing.

In response, applicants submit herewith as **Exhibit A,** a paper copy of the Sequence Listing, and request its entry into the specification. In addition, applicants annex hereto a C.R.F. Sequence Listing as **Exhibit B**, and a Statement in Accordance with 37 C.F.R. §1.821(f) as **Exhibit C**. Applicant maintains that the Sequence Listing attached hereto contains no new matter. Applicants further note that the sequence identifiers for the peptides on page 19 of the specification are already specified at page 19, lines 2-3.

The Examiner indicated that all references to Fig. 1, including the Brief Description, must indicate which panel of Fig. 1 is being referred to. The Examiner also indicated that "active" is misspelled on page 15.

In response, applicants have hereinabove amended the specification to refer to Fig. 1A or Fig. 1B as necessary and have corrected the inadvertent typographical error on page 15.

Claims Rejected Under 35 U.S.C. §112 (First Paragraph)

In the June 28 2006 Office Action the Examiner rejected claims 1-21 under 35 U.S.C. §112 as allegedly containing subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of the claimed invention. The Examiner stated that absent further written description and guidance from applicant, one would not know or be able to predict what other "agents" or immunogenic fragments of enolase specifically bind to the relevant autoantibodies and predictably function in the assay and kit to detect the relevant autoantibodies other than intact enolase, particularly intact neuron-specific or gamma enolase.

In response, applicants respectfully traverse the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have herein amended independent claims 1, 10, 16 and 19 to replace the term "agent" with "gamma enolase". Applicants note that the Examiner has indicated that such subject matter of claim is adequately described in the specification. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

The Examiner also rejected claims 1-21 under 35 U.S.C. §112 as not enabled by the specification in that applicant allegedly provides no description or guidance for what structure(s)/fragment(s) is(are) necessary and sufficient for function of the instant intact unmodified protein(s) itself in that a single change of an encoded amino acid unpredictably affects structure and function. The Examiner stated that only the disclosed specific full-length enolase proteins that bind to the relevant autoantibodies are enabled.

In response, applicants respectfully traverse the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have herein amended independent claims 1, 10, 16 and 19 to replace the term "agent" with "gamma enolase". Applicants note that the Examiner has indicated that such subject matter of claim is enabled by the specification. In addition, applicants note the examples of gamma enolase set forth in the specification at, inter alia, page 15, lines 16 to 27 as well as Figs. 21-24. With regard to the Examiner's assertions as to the structure and function of gamma enolase, applicants note that, in the context of the present in-vitro diagnostic test, the function of the gamma enolase is as a target autoantigen to selectively bind cognate autoantibodies. Consequently, such structures, and immunogenic fragments of gamma enolase, are readily determinable by one of skill in the art without resort to undue experimentation.

Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

The Examiner rejected claims 1-8 and 10-13 under 35 U.S.C. §112 as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of the claimed invention. The Examiner indicated that Hanson et al. (1992) and Gitlits et al. (1997) as disclosed in the Information Disclosure Statement filed March 4, 2005 in connection with the above-identified application suggest that autoantibodies specific for enolase are found in samples obtained from a variety of patients. The

Examiner further stated that the detection of such autoantibodies in a patient with Parkinson's or Alzheimer's disease, or in glaucomatous optic neuropathy, would not indicate neuropsychiatric systemic lupus erythematosus (NPSLE) in that patient. The Examiner further stated that absent further written description, one would not be assured of the ability to assess NPSLE in patients merely upon detection of the presence of autoantibodies in a sample from a patient not known or suspected of having systemic lupus erythematosus.

In response, applicants respectfully traverse the Examiner's rejection.

Initially, applicants note that Gitlits et al., 1997 as cited by the Examiner, is a case report which describes a patient with autoantibodies specific for *alpha*-enolase (non-neuronal enolase, ubiquitous enolase, ENO-1).

However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have herein amended independent claim 1, from which claims 2-9 depend, and independent claim 10, from which claims 11 to 13 depend, to recite that the subject is diagnosed with systemic lupus erythematosus but not neuropsychiatric systemic lupus erythematosus. As the Examiner has indicated, such subject matter is adequately described in the specification to show that the inventors, at the time the application was filed, were in possession of the claimed invention.

The Examiner rejected claims 1-8 and 10-13 under 35 U.S.C. §112, first paragraph, as allegedly not enabled by the specification.

The Examiner further stated that Hanson et al. (1992) and Gitlits et al. (1997) as disclosed in the Information Disclosure Statement filed March 4, 2005 in connection with the above-identified application suggest that autoantibodies specific for enolase are found in samples obtained from a variety of patients. The Examiner further stated that the detection of such autoantibodies in a patient with Parkinson's or Alzheimer's disease, or in glaucomatous optic neuropathy, would not indicate neuropsychiatric systemic lupus erythematosus (NPSLE) in that patient. The Examiner further stated that absent further guidance from applicant, one would not be able to assess NPSLE in patients merely upon detection of the presence of autoantibodies in a sample from a patient not known or suspected of having systemic lupus erythematosus.

In response, applicants respectfully traverse the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have herein amended independent claim 1, from which claims 2-9 depend, and independent claim 10, from which claims 11 to 13 depend, to recite that the subject is diagnosed with systemic lupus erythematosus but not neuropsychiatric systemic lupus erythematosus. As shown in the specification, e.g. at page 20, lines 1 to 12, patients with NPSLE showed immune reactivity to the purified 50kD protein, whereas patients with just SLE or with neuropsychiatric disease unrelated to SLE showed minimal reactivity. Accordingly, the presence of the autoantibodies in a patient known to have SLE is an indicator of the likelihood that the patient has NPSLE. In addition, applicants note that the references cited by the Examiner, namely Horvat et al. (Jugoslov. Med. Biohem., 16:217-219, 1997) and Maruyama et al. (Tohoku J. Exp. Med. 197:125-132, 2002) do not discuss or determine whether

the subjects tested had NPSLE. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claims Rejected Under 35 U.S.C. §112 (Second Paragraph)

The Examiner rejected claims 1 and 10 under 35 U.S.C. §112 (second paragraph) as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner stated that the term "likely" in the claims is a relative term which renders the claims indefinite.

In response, applicants respectfully traverse the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have herein amended claims 1 and 10 to remove the term objected to by the Examiner. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

The Examiner rejected claims 8, 14 and 15 in that the term "the amount" lacks antecedent basis. In addition, the Examiner stated that claim 9 is improperly dependent.

In response, applicants respectfully traverse the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have herein amended claims 8, 14 and 9 to address the Examiner's comments. Applicants note that claim 15 does not recite the term objected to by the Examiner. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of

rejection.

The Examiner rejected claim 19 in that the inter-relationships of the components recited in the claim are allegedly not clear because the agent is both bound and labeled.

In response, applicants respectfully traverse the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have herein amended claim 19 to delete the terminology relating to the agent being labeled.

Claims Rejected Under 35 U.S.C. §102(b)

The Examiner rejected claims 1-21 under 35 U.S.C. §102(b) as allegedly anticipated by Hanson et al. (J. Exp. Med. 176:565 (1992)). The Examiner stated that Hanson et al. detected autoantibodes in the sera of patients with systemic lupus erythematosus (SLE) and CNS involvement that bound an unidentified antigen of approximately 50 kD, inherently gamma enolase in light of the instant disclosure.

In response, applicants respectfully traverse the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have herein amended claims 1 and 10, on which claims 2-9 and claims 11-15 depend, respectively. Applicants note that Hanson et al. does not teach a method as recited in independent claims 1 and 10, of assessing if a patient diagnosed with SLE but not NPSLE is suffering from NPSLE. In addition, Hanson et al. does not provide kits for performing such, as recited in claims 16 and

19. Moreover, the identity of the 50kD paper was unknown in Hanson et al. and substantial experimental work was required to characterize bv the antigen. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

9/26/06

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